UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/584,207	11/28/2007	Terence J. Colgan	MCY5USA	3654

270 7590 10/12/2011

HOWSON & HOWSON LLP
501 OFFICE CENTER DRIVE
SUITE 210
FORT WASHINGTON, PA 19034

EXAMINER	
BORGEEST, CHRISTINA M	

ART UNIT	PAPER NUMBER
1649	

NOTIFICATION DATE	DELIVERY MODE
10/12/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@howsonandhowson.com

Office Action Summary	Application No.	Applicant(s)	
	10/584,207	COLGAN ET AL.	
	Examiner	Art Unit	
	CHRISTINA BORGEEST	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *2-4,6,9,19 and 50-54* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☐ Claim(s) _____ is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☒ Claim(s) *2-4,6,9,19 and 50-54* are subject to restriction and/or election requirement.

Application Papers

10)☒ The specification is objected to by the Examiner.

11)☒ The drawing(s) filed on *23 June 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/23/2011; 7/12/2011*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2 June 2011 has been entered.

Claims 2, 3, 9 and 19 are amended. Claims 50-54 are new. Claims 8, 20 and 21 are newly cancelled. Claims 2-4, 6, 9, 19 and 50-54 are under examination.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) and 365(c) is acknowledged. Based on the information given by Applicant and an inspection of the prior applications, the Examiner has concluded that the subject matter defined in the instant claims is supported by the disclosure in provisional application serial no 60/532,601, filed on 23 December 2003 and provisional serial no. 60/630,990 filed on 24 November 2004, because the claimed invention is disclosed in said applications. In addition, the subject matter defined in the instant claims is supported by the disclosure in PCT/CA2004/002172. Thus, the priority date of claims 2-4, 6, 9, 19 and 50-54 of the instant application is deemed to be 23 December 2003.

Rejections Withdrawn

Note: All previous rejections over claims 8, 20 and 21 are hereby withdrawn in response to Applicant's cancellation of those claims.

Claim Rejections - 35 USC § 102/35 USC § 103

The rejection of claims 2-4 and 9 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Warrington et al., 2001/0044104, published 22 November 2001 in view of zellnet.com/nss-folder/pictures/Fig1.gif, downloaded 8 March 2010 is withdrawn in response to Applicant's amendment of the claims to recite "wherein an elevated or increased level or amount of human chaperonin 10 in the biological sample, relative to the corresponding level or amount in the control, is indicative of endometrial cancer." Specifically Warrington et al. teach at Table 6 that chaperonin 10 is differentially expressed by "4 fold", but does not indicate whether the levels are up- or down-regulated. Further, paragraph [0034] of Warrington et al., teaches that the term “differentially expressed” as used therein means that the measurement of a cellular constituent varies in two or more samples and that the cellular constituent can be either up-regulated in the experimental relative to the reference or down-regulated in the experimental relative to the reference. In the absence of any clear teaching in Warrington et al. as to whether chaperonin 10 is up- or down-regulated, the rejection(s) under 35 U.S.C. 102(b), or in the alternative, 35 U.S.C. 103(a), cannot be maintained.

Rejections Maintained/New Rejections/Objection

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. The hyperlinks are found at p. 104 and 109. Note that this objection could be overcome by amending the links slightly, for instance, at p. 104, line 33, the NCI website could read: bc.cancer.ca/vgn/images/portal/cit.sub.--776/61/38/56158640niw-_stats_en.pdf.

Claim Rejections - 35 USC § 112, first paragraph

Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 2-4, 6 and 9 under 35 U.S.C. 112, first paragraph, for scope of enablement is maintained for the following reasons. It is noted that most of the issues raised by the Examiner in the previous Office actions have been overcome by Applicant's amendment. However, there is one remaining issue discussed herein. The specification, while being enabling for a method of screening for an endometrial cancer in a subject comprising (a) detecting the level or amount of human chaperonin 10 in a biological sample obtained from the subject, wherein the human chaperonin 10 has an amino acid sequence set forth in SEQ ID NO: 1 and wherein the biological sample is

endometrial tissue sample; and (b) comparing the level or amount in step (a) with a level or amount of human chaperonin 10 in a control endometrial tissue sample, wherein an elevated or increased level amount of human chaperonin 10 in the endometrial tissue sample from the subject relative to the corresponding level or amount in the control, is indicative of endometrial cancer, does not reasonably provide enablement for an amino acid sequence having at least 90% sequence identity to the sequence set forth in SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." (See In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 Fed. Cir. 1988) These factors include, but are not limited to: (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

(i) Chaperonin 10 is defined in the specification at p. 17, lines 13-17 in the following way:

> The term "chaperonin 10", "chaperonin 10 polypeptide" or "chaperonin protein" includes human chaperonin 10, in particular the native-sequence polypeptide, isoforms, chimeric polypeptides, all homologs, fragments, precursors, complexes, and modified forms and derivatives of human

chaperonin 10.

The specification does not provide any specific examples of chaperonin 10 mutants that could be used in the claimed proteomic assay. Considering that the invention contemplates measuring chaperonin 10 levels by proteomic methods as a marker for endometrial cancer, it is important that the test be accurate with the highest possible level of sensitivity and specificity. It is known that chaperonin 10 need only differ from wild-type by a single residue to be destabilizing. Note Brown et al. (Archives of Biochemistry and Biophysics, 2005; 439: 175-183) teaches two mutations at p. 181, left column:

> When the non-conserved valine-100 in the β-strand is replaced by glycine, the resulting protein remains heptameric although it exhibits somewhat lower thermodynamic stability as compared to wild-type cpn10. In sharp contrast, when the conserved phenylalanine-8 in the N-terminal-strand is replaced by a glycine, this mutation both unfolds the resulting protein and dissociates the heptamer into mostly monomers.

Brown et al. also teaches the Leu96Gly mutation in chaperonin 10 at p. 181, right column:

> Despite the native-like subunit–subunit affinity, the overall thermodynamic stability towards both chemical and thermal perturbations of the Leu96Gly cpn10 heptamer is dramatically decreased as compared to wild-type cpn10.

In addition, Brown et al. teaches that chaperonin 10 has a role in carcinogenesis and that despite high homology across species, there are vast immunogenic differences and it still not understood what part of the structure of chaperonin 10 plays a role in in these immunogenic divergences (see p. 176, left column). Brown concludes at p. 183:

> In contrast to bacterial GroES [the bacterial chaperonin 10 homolog], ***a monomeric equilibrium intermediate has never been observed during***

> ***equilibrium unfolding/disassembly of any human cpn10 variant***. This may be a reflection of minor sequence divergences at the interface; the existing data on human cpn10 variants demonstrate that unfolding/dissociation mechanisms can be altered by single amino-acid changes. As a consequence, ***the structural states populated by cpn10 proteins in vivo at various conditions will vary between species; this may be associated with divergent non-chaperonin activities***. (Citations omitted by Examiner; emphasis added by Examiner).

Thus, it is clear from the art that much remains to be discovered about how changes in the primary chaperonin 10 structure affects its tertiary and quarternary structure, and thus, function.

Given that the invention encompasses measuring chaperonin 10 levels by proteomic methods as a marker for endometrial cancer, it is important that the test be accurate with the highest level of sensitivity and specificity. A test that can detect any isoform, chimeric polypeptide, homolog, fragment or modified form of chaperonin 10 would sacrifice a great deal in specificity. One skilled in the art would be required to undergo undue experimentation to identify those chaperonin 10 mutein measurements that accurately predict cancerous or non-cancerous endometrium. This is further complicated by the fact that proteomics technology is complex and unpredictable. Note the news report by Erika Check (Nature, 2004; 429: 496-497—on Applicants' 1449 form), which explains that the field has not yet had the opportunity to develop standards for interpreting test results. An illustrative example is given regarding internal inconsistencies in the data of an early detection test for ovarian cancer. The issue regarding the unpredictability of structural mutations of chaperonin 10 is exacerbated given the complexity and unpredictability of proteomics.

Generally speaking, the number of mutations possible in any given protein that

can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. See Tokuriki and Tawflik, (Current Opinion in Structural Biology 2009, 19: 596-604), who teach that mutations are generally destabilizing. For instance, Tokuriki and Tawflik teach at p. 596, right column, last paragraph, that "as mutations accumulate, protein fitness declines exponentially...or even more than exponentially...So by the time an average protein accumulates, on average, five mutations, its fitness will decline to <20%." Further, at p. 598, left column, last paragraph, Tokuriki and Tawflik notes that 50% of mutations are destabilizing, and >15% of mutations are highly destabilizing, and of the about 5% of mutations that are stabilizing values...many of these mutations result in inactive protein. This is further underscored by the discussion by Brown, in the preceding paragraphs, who teach that only a single mutation in chaperonin 10 is destabilizing. Indeed, Tokuriki and Tawflik conclude that "a more comprehensive understanding of how mutations affect protein fitness within living cells is needed, including their combined effects on function, thermodynamic and kinetic stability, and clearance through aggregation and degradation" (see p. 602, left column, 2nd paragraph), thus one skilled in the art would face serious challenges due to the lack of predictability with regard to the effects of mutation on the ability of chaperonin 10 to predict endometrial cancer in a proteomic assay.

Applicants have provided little or no guidance beyond the mere presentation of

sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins (pages 17-18 of the specification, for instance), this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation.

Due to the large quantity of experimentation necessary to determine which chaperonin 10 muteins can be detected in endometrial tissue and be shown to be differentially expressed between those patients with and without endometrial cancer and to therefore accurately predict said endometrial cancer, the lack of direction/guidance presented in the specification regarding the same; the absence of working examples directed to the same; the complex nature of the invention; the unpredictable state of proteomics technology and its ability to accurately predict cancer; (the level of skill of those in the art); and the breadth of the claims which fail to recite limitations on the structure of the chaperonin 10 mutein, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Total Lack of Enablement

The rejection of claim 19 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is maintained for reasons of record and the

following. ***Further, new claims 50-54 are hereby included in this rejection.*** The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." (See In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 Fed. Cir. 1988) These factors include, but are not limited to: (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

(a) The goal of claims 19 and 50-54 are to monitor the progression of endometrial cancer (claim 19) comprising comparing levels or amounts of chaperonin 10 in a subject to the chaperonin 10 levels or amounts at an earlier point in time, wherein an elevated or increased amount indicates progression of endometrial cancer. It is noted that the specification does not teach that the levels of chaperonin 10 rise over time in such a way that they can indicate progression of endometrial cancer. Rather, the examples teach that the relative protein levels of chaperonin 10 in endometrial tissue from endometrial cancer patients are higher with respect to controls. Further, paragraph [0439] teaches that 5/22 or 23% of cancer subjects had undetectable levels

of chaperonin 10, thus indicating that the current test does not even detect chaperonin 10 in all of the possible cases of endometrial cancer. Furthermore, the techniques used to detect relative protein levels in the specification are semi-quantitative. There is no teaching that chaperonin 10 levels rise in such a way to predict progression of disease, which would be required if one was to use the tests not merely to screen for the possibility of endometrial cancer, but also to monitor its progression. Tables 2 and 3 only show measurements in terms of intensity of expression. The specification does not provide a nexus between these protein measurements and the stage of endometrial cancer, cancer aggressiveness, or whether the cancer has or will metastasize. The more detailed methods of monitoring progression of the disease require one skilled in the art to undertake empirical research to establish how chaperonin 10 levels are predictive of a particular stage of disease. Finally, recent work by the inventors (Yang et al. and Dube et al.—both of record) do not teach the existence of pre-determined standards or cut off values that would enable one skilled in the art to undertake the more detailed methods of monitoring progression of endometrial cancer, i.e., correlating a particular level of chaperonin 10 with a particular stage of endometrial cancer. The methods recited in claims 19 and 50-54 represent an invitation to the skilled artisan to undertake further research to discover the parameters needed to carry out the goal of the recited methods. Furthermore, proteomics technology is complex and unpredictable. Note the news report by Erika Check (Nature, 2004; 429: 496-497—on Applicants' 1449 form), which explains that the field has not yet had the opportunity to develop standards for interpreting test results. An illustrative example is given

regarding internal inconsistencies in the data of an early detection test for ovarian cancer. Given the complexity and unpredictability of the technology, Applicant is not enabled for correlating a particular level of chaperonin 10 with a particular stage of endometrial cancer, as the claims require.

(b) Furthermore, even if Applicant were enabled for claims 19 and 50-54, the issue raised in the preceding rejection under 35 U.S.C. 112, first paragraph over claims 2-4, 6 and 9 in point (i) above are also applicable here and are hereby incorporated.

Due to the large quantity of experimentation necessary to determine values of chaperonin 10 that would be capable of monitoring progression of disease as recited in the claims, the lack of direction/guidance presented in the specification regarding the same; the absence of working examples directed to the same; the complex nature of the invention; the unpredictable state of proteomics technology and its ability to accurately predict cancer, (the level of skill of those in the art); and the breadth of the claims which fail to recite limitations on the chaperonin 10 mutein, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

Written Description

Claims 2-4, 6, 9, 19 and 50-54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention. The claims recite methods of detecting levels of human chaperonin 10 in an endometrial sample, wherein the human chaperonin 10 has an amino acid sequence having at least 90% sequence identity to the sequence set forth in SEQ ID NO: 1.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of 90% percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. The specification fails to disclose and there is no art-recognized correlation between the structure of the genus of chaperonin 10 polypeptides and their function in the claimed methods of diagnosis and prognosis. As noted above, the art teaches that chaperonin 10 can vary by only a single amino acid to result in an unfolded and inactive protein (see Brown et al. and discussion in preceding rejection under Scope of Enablement, hereby incorporated). Thus minor changes in primary amino acid structure can have debilitating effects on tertiary and quartenary structure, and thus function. In addition, the specification does not teach which 10% of the amino acids can vary from SEQ ID NO: 1 and still result in a protein that retains the

ability to function in the recited methods. Finally, the specification fails to provide adequate written description in the form of structure and/or structure-to-function characteristics that demonstrate possession of the encompassed genus of any protein having at least 90% homology to SEQ ID NO: 1. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). With the exception of SEQ ID NO: 1, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

The full breadth of the claims encompass a broad genera including proteins that are homologous to human chaperonin 10 but that lack the correct tertiary and quarternary structure, and thus activity. One cannot describe what one has not

conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO: 1, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Response to Arguments

Applicant asserts at p. 6, 3rd paragraph and p. 7, 2nd paragraph that, in addition to the claimed method being enabled for detecting a chaperonin 10 having the sequence set forth in SEQ ID NO: 1, the claimed method is also enabled for detecting chaperonin sequences having at least 90% identity to SEQ ID NO: 1, citing the instant specification at pages 17 and 18.

This argument has been fully considered but is not found persuasive. The cited pages in the instant specification do not provide any specific examples of variants, but rather just provide broad definitions of variants. For instance, at p. 17, beginning line 31:

> Such variants include, for instance, polypeptides wherein one or more amino acid residues are added to, or deleted from, the N- or C-terminus of the full-length or mature sequences of the polypeptide, including variants from other species, but excludes a native-sequence polypeptide. In aspects of the invention variants retain the immunogenic activity of the corresponding native-sequence polypeptide.

This is merely an invitation to the skilled artisan to discover those variants which can be used in the claimed methods. As noted above, Brown et al. teaches that despite high

homology of chaperonin 10 across species, there are vast immunogenic differences and it still not understood what part of the structure of chaperonin 10 plays a role in divergences (see p. 176, left column). Brown concludes at p. 183:

> In contrast to bacterial GroES [the bacterial chaperonin 10 homolog], ***a monomeric equilibrium intermediate has never been observed during equilibrium unfolding/disassembly of any human cpn10 variant***. This may be a reflection of minor sequence divergences at the interface; the existing data on human cpn10 variants demonstrate that unfolding/dissociation mechanisms can be altered by single amino-acid changes. As a consequence, ***the structural states populated by cpn10 proteins in vivo at various conditions will vary between species; this may be associated with divergent non-chaperonin activities***. (Citations omitted by Examiner; emphasis added by Examiner).

Thus, it is clear from the art that much remains to be discovered about how chaperonin 10 structural variants affect their function. For this reason, the specification, which does not provide any clear guidance as to how changes in primary chaperonin 10 structure affect its tertiary and quarternary structure, does not provide sufficient guidance for 90% of SEQ ID NO: 1 in the absence of any guidance in the literature.

Applicant asserts at p. 7, 3rd paragraph, that the claims now recite that chaperonin 10 is measured at two time intervals wherein the progression of cancer is indicated when the level or amount at the second time interval is greater than at the first measurement, stating that such would be recognized by the skilled artisan.

This argument has been fully considered but is not found persuasive. As indicated above, the specification does not teach that the levels of chaperonin 10 rise over time in such a way that they can indicate progression of endometrial cancer. Rather, the examples teach that the relative chaperonin 10 protein levels in endometrial tissue from endometrial cancer patients are higher with respect to controls, thus the techniques are semi-quantitative. Further, paragraph [0439] of the instant PG PUB

teaches that 5/22 or 23% of cancer subjects had undetectable levels of chaperonin 10, thus indicating that the current test does not even detect chaperonin 10 in all of the possible cases of endometrial cancer. There is no teaching that chaperonin 10 levels rise in such a way to predict progression of disease, which would be required if one was to use the tests not merely to screen for the possibility of endometrial cancer, but also to monitor its progression. Tables 2 and 3 only show measurements in terms of non-quantitative intensity of expression, and there is no comparison between earlier and later measurements in time in endometrial cancer patients. The specification does not provide a nexus between these protein measurements and the stage of endometrial cancer, cancer aggressiveness, or whether the cancer has or will metastasize. Thus the claims are not enabled for methods of monitoring progression.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRISTINA BORGEEST whose telephone number is (571)272-4482. The examiner can normally be reached on 9:00am - 3:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Daniel Kolker can be reached on 571-272-3181. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christina Borgeest
/Christina Borgeest/
Examiner, Art Unit 1649